



Research Article

ROS Influence in Oral Ulcer Occurrence, Number and Types in Systemic Lupus Erythematosus Patients

Mohammed Faris Jabaz

Department of Dentistry, Al-Mustaqbal University College, Iraq

KEY WORDS:

ROS
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Abstract:

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by oral ulcer (Ou) as one of the SLE manifestations, some factors are contributed in SLE etiology, Reactive oxygen species (ROS) are one of these factors. A cross sectional study aim to evaluate the ROS role in oral ulcer occurrence, number and types in SLE patients. The results demonstrate significant changes in age, non-sig in BMI and patients duration average was 6.87 years. The ROS level showed significant-elevation in SLE group ($p = 0.000$). Patients classified according to oral ulcer occurrence results found high percentage of patients have Ou (72.60)% with non-sig changes in age, BMI, duration and ROS level. finding also showed (48.4%) of patients have single Ou, low percentage (24.3%) have multiple Ou and (27.4%) without Ou with non-sig changes in all study variation and slightly elevation of ROS in a single ulcer, five types of oral ulcer including mouth, lips, tongue, pharynx and gum, high percent of patients have mouth ulcer (33.9%), then tongue (14.5%) and low percent was observed in lips (3.9%) and variables have non-sig changed, ROS was elevated in mouth Ou and decreased in lips oral Ou, other types have slightly changes in compare with patients without Ou, The ROS levels in each oral ulcer types in compare with patient without this types didn't significant associated with ROS levels ($p = 0.143, 0.366, 0.394, 0.471, 0.729$) for mouth, lips, tongue, pharynx and gum respectively. the current finding proved robust association of SLE with ROS level but non-significant relation with oral ulcer incidence, type and number in SLE patients.

Corresponding Author:

Mohammed Faris Jabaz

Department of Dentistry, Al-Mustaqbal University College, Iraq

INTRODUCTION

Systemic lupus erythematosus (SLE) the clinical heterogeneity and an autoimmune disease with complex

etiology that explained by some studies via a series of aspects to facilitate early diagnosis to avoid severe complications, many factors interplaying contributed in

SLE incidence like genetic, epigenetic and environmental factors (Fortuna and Brennan^[2], Weinstein^[3]). Many investigations have found that the oral manifestations are the first signs and symptoms appear among other symptoms, thus it's important to understand the factors may impact in oral ulcer (Fortuna and Brennan^[2], Narváez^[1]).

Free radicals are natural production of some biological processing which have high reactivity belong to the presence of a spilled electron (Halliwell B, Gutteridge^[4]). This chemical features make their instable thus, the urgency to react with other molecules. During short existence of radical, its captured an electron from other molecules, lead to chain reaction that cause chemical structure alteration of the cellular compartment. The most cellular component exposed to the adverse impacts of free radicals are low-density lipoproteins, proteins lipid structures and DNA and RNA (Hua^[5]), consequences the products of these interaction is responsible of oxidative damage.

Free radicals are generated through vital processing as well as ATP synthesis, tissue repair and immune reactions (Giorgio^[6], Finkel^[7]), in addition to chronic exposure to ionizing radiation and to chemical compound like drugs, pollutants, pesticides, cigarette smoking and prolonged stress (Ichiishi^[8], Helmersson^[9]). Its contributed in some disease if stresses don't neutralize, these highly reactive molecules causes damage cell components and stimulate mutations involved in the several diseases pathogenesis. Oxidative stress have significant impacts in the aging process acceleration and in the chronic and degenerative diseases development (Lithgow and Walker^[11], Hong^[10], Phaniendra^[12]).

An aberrant free radicals generation implicated in the several pathologies onset like, autoimmune disorders, arthritis cataract, cancer, retinitis pigmentosa, cardiovascular and neurodegenerative disorders (Rodrigo^[17], Banarjee and Mukhopadhyay^[13] Thiagarajan and Manikandan^[14], Tarafdar and Pula^[15], Perdices^[16]). Its induced uncontrollable autoimmune diseases and central nervous system pathologies, like Alzheimer's dementia and Parkinson's disease (Halliwell^[18], Buczko^[19]).

The information form previous reports pointed the direct association between levels of free radical, oxidative stress and inflammatory states. That observed in several common inflammatory diseases and potential neoplastic lesions of the oral cavity (Bagan^[20], Racz^[21]). Inflammatory diseases contributing in the oral cavity impact about 50% of the adult population. They consist in the gingival tissue reduction and in the some severe cases, retraction of the underlying bone tissue, which observed in 10-15% of the population in the world (Sculley^[22], Brown^[23]).

MATERIALS AND METHODS

Study Subjects: the present study was proposed to evaluate the ROS role in the oral ulcers features in SLE patients, A case- control study included 60 patients and 50 healthy individuals, patients were attended to Marjan hospital city for medication, all patients were diagnosed by specialist physician and oral ulcer were detected by dentist specialist to diagnose the ulcer features.

Data and Sample Collection: data and blood samples were collected from study subjects with written consent and according to the ethical approval of ministry of higher education and scientific research, blood samples were collected for serum isolation, then ROS level was detected using

Reactive oxygen species (ROS) were evaluated according to the FOX2 method^[12]. The FOX2 test system is based on the oxidation of ferrous ion-odanisidine complex to ferric ion by the differnt types of oxidants contained in the plasma samples. The Fe(III) ion produced is bound by xylenol orange, construct a complex with an absorption peak at 560 nm.

Data Analysis: results were analyzed via SPSS V23, mean±SE was used to demonstrate results, independent t test and ANOVA one way used for significant detection at $p < 0.05$.

RESULTS AND DISCUSSIONS

The present study demonstrate the Influence of ROS in oral ulcer characterization companies with SLE

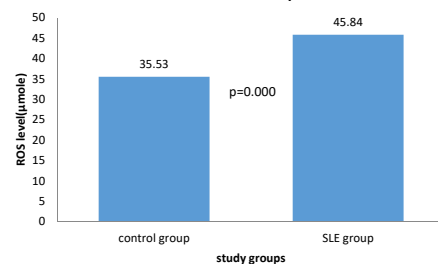


Fig. 1: ROS levels in study groups (mean±SE)

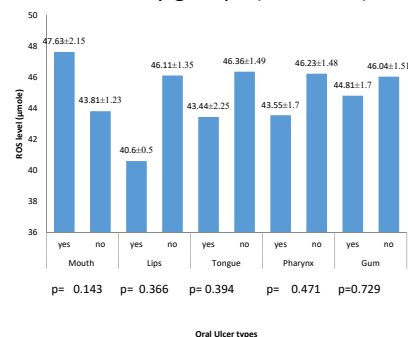


Fig. 2: The ROS level in the patients with and without different type of oral ulcer

Table 1: Study variation distribution according to study groups (patient v control).

Subjects	Control group	SLE group	P
Age (year)	35.82±1.41	31.32±1.05	0.015*
BMI(kg/m ²)	28.16±0.94	26.81±0.50	0.233
Duration(year)	6.87±0.82	-	-

Independent sample t test p <0.05. (mean±se)

Table 2: Study variations distribution according present of oral ulcer.

Subjects	With ulcer	Without ulcer	P
Percentage %	72.6	27.4	-
Age (year)	37.31±1.60	32.05±2.78	0.102
BMI(kg/m ²)	28.54±1.17	27.75±1.48	0.795
Duration(year)	7.82±1.03	4.44±1.05	0.068
ROS (μmole)	43.71±1.12	45.72±1.89	0.953

Independent sample t test p <0.05. (mean±se)

Table 3: Study variation distribution according to number of oral ulcer

Subjects	Single ulcer	Multiple ulcer	Without ulcer	P
Percentage %	48.4%	24.2%	27.4%	-
Age (year)	39.23±2.12	33.26±1.95	32.05±2.78	0.060
BMI(kg/m ²)	28.86±1.58	27.22±1.66	27.75±1.48	0.764
Duration(year)	8.16±1.32	7.08±1.65	4.44±1.05	0.166
ROS (μmole)	46.75±2.27	44.18±1.96	45.72±1.89	0.733

ANOVA one way, mean±SE p <0.05

Table 4: Study variations distribution according to types of oral ulcer

Subjects	Mouth	lips	Tongue	Pharynx	Gum	Without ulcer	p
Percentage %	39.5%	3.9%	14.5%	9%	13.2%	22.4%	-
Age (year)	36.54±2.03	37.66±4.63	37.00±2.38	33.22±3.34	35.40±2.62	32.05±2.78	0.753
BMI(kg/m ²)	28.26±1.44	32.18±5.49	27.16±2.02	30.90±2.11	25.51±1.61	27.75±1.48	0.881
Duration(year)	7.12±1.16	5.66±3.28	9.63±2.47	5.13±1.84	7.80±1.90	4.44±1.05	0.369
ROS (μmole)	47.63±2.15	40.60±0.50	43.44±2.25	43.55±1.73	44.81±1.75	45.72±1.89	0.654

ANOVA one way, mean±SE p <0.05

patients, the finding show significant changes in age, non-sig in BMI and duration average 6.87 years (table 1). The ROS level showed significant-elevation in SLE group (p = 0.000) figure(1).

The SLE patient group classified according to the oral ulcer existing to present and absent oral ulcer, high percentage of patients have Ou (72.60)%, non-sig changes observed in age, BMI, duration and ROS level between both groups. Taking into consideration, Ou observe in patients have long disease duration (7.82) years (table 2).

The SLE patients categorized according to the number of oral ulcer to the single, multiple and patients without Ou, finding showed about (48.4%) of patients have single Ou, low percentage (24.3%) have multiple Ou and (27.4%) without Ou, non-sig changes were found in all study variation and slightly elevation of ROS observed in single ulcer (table 3).

In the present study, five types of oral ulcer were found including mouth, lips, tongue, pharynx and gum, high percent of patients have mouth ulcer (33.9%), then tongue (14.5%) and low percent was observed in lips (3.9%). All study variables have non-sig changed, ROS was elevated in mouth Ou and decreased in lips oral Ou, other types have slightly changes in compare with patients without Ou (table 4).

The ROS levels in each oral ulcer types in compare with patient without this types also reported in the

study, all types didn't significant associated with ROS levels (p = 0.143, 0.366, 0.394, 0.471, 0.729) for mouth, lips, tongue, pharynx and gum respectively figure (2).

The current study found strong association of ROS with SLE disease, previous report proved that ROS have significant role in SLE via cellular signaling and adverse effects in cell components as well as proteins, lipid and DNA lesions (Campbell^[24], Kienhöfer^[25]). Some Clinical symptoms of SLE induced by ROS include malaise, fever, headaches, appetite and weight changing. The joint disorders, oral ulcers and renal problems (Smith and Gordon^[26]). Present result didn't agree with report implemented by Bengtsson^[27] who proved low ROS production in in granulocytes of SLE patients, while its agreed with Shruthi^[28] who found that SLE have high level of oxidative stress represented by Malondialdehyde, 8-hydroxy-2-deoxyguanosine and low total antioxidant level and associated with some disease manifestations and overall disease activity.

Regarding to the oral ulcer, different types and number were reported in the study, early investigations pointed that Oral ulcer is one of the most mucosal involvement features in about of 7%-52% SLE and used as SLE diagnostic criteria (Sultan^[29]), the buccal mucosa, vermilion border and hard palate are the most common involved location. Almost cases have painless ulcer, about 82% of SLE patients had painless ulcers (Urman^[32], Raymond^[34]), while some other studies had reported

painful ulcers in a higher frequencies (Jonsson^[33]) This because variation among types of oral ulcer. Oral ulcers may be happened by infections, aphthous stomatitis, or side effects of medication.

There are several risk factors involved in ulcer development in SLE patients such as smoking, Raymond et al found in a cross-sectional study that SLE patients who smoked had higher odds of mucosal ulceration in significant differences (Raymond^[34]). Oral lesions and ulcers have been more prevalent in severe disease cases, in SLE its linked to the overall activity and organ-related processes (Urman^[34]). but it unrelated to systemic complement or autoantibody levels (Takeno and Ishigatsubo^[34]).

Unfortunately, poor information about oral ulcers and SLE outcomes. its reported as an efficient predictors of worse prognosis and systemic vasculitis (Nico^[36]).

The role of ROS in oral ulcer of SLE patients didn't well study, however some studies proved ROS implicated in oral disease like recurrent aphthous stomatitis (Ghasemi^[37]), Oral Mucosal Diseases (Sardaro^[38]), on the other hand, the effect of the ROS in tissue represented by protein oxidation, lipids peroxidation and DNA lesions that lead to tissue injury and may be contributed in ulcers. In spite of non-significant association between ROS level and oral ulcer number, types and incidence, indirect relation may be contributed in oral ulceration by ROS regarding to closed relation of ROS with SLE.

CONCLUSION

The current finding proved robust association of SLE with ROS level but non-significant relation with oral ulcer incidence, type and number in SLE patients.

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